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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,173	07/11/2003	Zijian Guo	CITI350-2	8237

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Lisa A. Haile, J.D., Ph.D.
GRAY CARY WARE & FREIDENRICH LLP
Suite 1100
4365 Executive Drive
San Diego, CA 92121-2133

EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 02/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/618,173	GUO ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 49-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Attached Sequence alignment*.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 11/18/05, is acknowledged.

2. Claims 1-4 and 49-51 are pending and under examination.

3. In view of the amendment filed on 11/18/05, only the following rejections are remained.

3. The following new ground of rejections are necessitated by the amendment submitted 11/8/05.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-4 and 49-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a purified polypeptide comprising **the** amino acids of SEQ ID NO:2 for delay cell cycle progression; does not reasonably provide enablement for a substantially pure polypeptide characterized as (a) phosphorylating Cdc25 or a "homologue thereof" , having "about" 517 amino acid in claims 1 and 49, wherein the polypeptide has "an" abmino acids sequence as set forth in SEQ ID NO: 2 in claims 2 and 50, or a substantially pure polypeptide having "an" amino acid sequence as set forth in SEQ ID NO: 2 or "conservative variants thereof" in claim 3 or a substantially pure polypeptide "having" 'an" amino acid sequence that is "about 80% homologous to the polypeptide of SEQ ID NO: 2 in claim 4, or a substantially pure polypeptide having "an amino acid sequence" as set forth in SEQ ID NO: 2 in claim 51. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action mailed 08/25/05.

Further, claim 51 recites a polypeptide has "an" amino acid sequence as set forth in SEQ ID NO:2. However, the term "has" is open ended. In the absence of an explicit definition that imposes some lower limit on the size of what is encompassed by the "polypeptide" in the specification, the claimed polypeptide encompasses any sequence of three or more amino acids fully contained within SEQ ID NO: 2. The specification has not enabled such polypeptides. While in claims 1-2 and 49-50 the claimed polypeptides encompass any sequence having "about 517 amino acids". Besides **the** polypeptide of SEQ ID NO: 2, the specification fails to provide sufficient guidance on the size of what is encompassed by the term "about".

Applicant's arguments, filed 11/18/05, have been fully considered, but have not been found convincing.

Applicant argues that the specification provides enough guidance with respect to Cdc25, practicing the invention with respect to the homologues and conservative variants of Cdc25 would require no more than minor variations of what is described. Devising such minor variation are not more than common tasks routinely performed by competent researchers. Applicant submits that in view of the definition of "homology" on page 10 of the specification, those having ordinary skill in the art would understand that the structure of the homologues of Cdc25 is very similar to that of Cdc25. Applicant concludes that similar properties of Cdc25 and of the homologues are expected. Further, teaching how to practice the invention with respect to Cdc25 would also inherently teach how to practice the invention with respect to the homologues.

However, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases and recognized that it was unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences. Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are echoed by Doerks et al (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the databases, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

Applicant submits that the specification also define "conservative variants" and those having ordinary skill in the art would understand that the biological properties of such conservatives variants of a polypeptide that comprises SEQ ID NO:2 would be very similar to the biological properties of the purified polypeptide itself. Applicant concludes that teaching how to practice the invention with respect to the purified polypeptide would also inherently teach how to practice the invention with respect to its conservative variants.

However, there is tremendous variability in the importance of individual amino acids in protein sequences. Since the FHA domain, SQ/TQ motifs and carboxyle terminal kinase domain are key determinants of activity of claim SEQ ID NO:2, residue substitutions that are conservative (e.g., Glu in equilibrium Asp, Asn in equilibrium Asp, Ile in equilibrium Leu, Lys in equilibrium Arg

and Ala in equilibrium Gly) can have severe phenotypic effects. There is no simple way to infer the likely effect of an amino acid substitution on the basis of sequence information alone. Therefore, one skill in the art would not be able to predicted what residue substitutions can be replaced.

6. Claims 1-4 and 49-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a purified polypeptide comprising the amino acids set forth in SEQ ID NO:2 for delay cell cycle progression.

Applicant is not in possession of a substantially pure polypeptide characterized as (a) phosphorylating Cdc25 or a "homologue thereof" , having "about" 517 amino acid in claims 1 and 49, wherein the polypeptide has "an" abmino acids sequence as set forth in SEQ ID NO: 2 in claims 2 and 50, or a substantially pure polypeptide having "an" amino acid sequence as set forth in SEQ ID NO: 2 or "conservative variants thereof" in claim 3 or a substantially pure polypeptide "having" 'an" amino acid sequence that is "about 80% homologous to the polypeptide of SEQ ID NO: 2 in claim 4, or a substantially pure polypeptide having "an amino acid sequence" as set forth in SEQ ID NO: 2 in claim 51 for the same reasons set forth in the previous Office Action mailed 08/25/05.

Applicant's arguments, filed 11/18/05, have been fully considered, but have not been found convincing.

Applicant argues that the specification clearly discloses that the Applicants in possession of both pure polypeptides having the SEQ ID NO: 2 and of conservative variants thereof. Applicant argues that the specification further discloses that the Applicants were in possession of polypeptides capable of phosphorylating both Cdc25 and homologues thereof.

However, there is no described or art-recognized correlation or relationship between the structure of the invention, the carboxyl terminal kinase domain, FHA domain, and the SQ/TQ motifs of claimed SEQ ID NO: 2 and it's delay cell cycle progression function, the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of variants including conservative variants, wherein the variant has at least 80% homologous with SEQ ID NO:2, which retain the features essential to the instant invention. Further, the specification fails to describe the amino acids that get phosphorylated by claimed SEQ ID NO:2 let alone a homologue thereof.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-4 and 49-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Matsuoka et al (science 282:1893-1897, 1998).

Matsuoka et al teach a ChK2 polypeptide characterized as (a) phosphorylating Cdc25 on sering-216 (see abstract in particular), (b) having a molecular mass of 60 kD (i.e., about 58 kD) (see Fig 2 in particular), (c) having 543 amino acids (i.e., about 517 aa) (see (Fig. 1A in particular), having SQ/TQ motifs at the amino terminal region (see Fig. 1A, aa19-69 in paricular), having a carboxyl terminal kinase domain (see Fig1A and Fig1 C, and aa 226-486 in particular) and (f) having an amino acid forkhead-associated domain (FHA) (see Fig1A in particular). The product of the instant claims are defined in terms of physical characteristics rather than by structure. Consequently, comparison of the instant products with prior art is difficult since the Office is not equipped to manufacture the claimed product and/or prior art products that appear to be related and conduct comparisons. In consideration of the discrepancies often encountered in the art between protein molecular weight when determined by different methods, when a molecular weight is recited to characterize a protein the claims should include not only the method by which it was determined, e.g. whether by sodium dodecyl sulphate polyacrylamide gel electrophoresis, gel filtration or some other method, but also whether the determination was made under denaturing or non-denaturing conditions and whether reducing or non-reducing conditions were are used. The burden is on the applicant to establish a patentable distinction between the claimed and referenced polypeptide. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

Claim 51 is included because a polypeptide having "an" amino acid sequence set forth in SEQ ID NO:2 can encompass as little as three amino acid, and several amino acid sequence with at least 3 amino acids occur at least once in the Chk2 polypeptide taught by Matsuoka et al, this claim encompasses any and all isolated polypeptides with at least 3 amino acid stretch of the sequence of SEQ ID NO: 2 (see attached sequence alignment). The term "having" in claim 50 is open-ended, it would open the claim to include the 543 amino acid sequence taught by Matsuoka et al.

Claims 2-3 and 50 are included for the reasons set forth for claim 50, in addition, the referenced 543 amino acids are "about" 517 amino acids.

The reference teachings anticipate the claimed invention.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The

fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 24, 2006

Maher Haddad

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600